

APPRAISAL

on the competition for the academic position "Associate Professor" in the professional field 4.3. Biological Sciences (Crystallization and Structural Analysis of DNA and Proteins) for the needs of the "Structural Crystallography and Material Science" department at the Institute of Mineralogy and Crystallography "Acad. Ivan Kostov", Bulgarian Academy of Sciences (BAS), announced in the "State Gazette" issue No. 95, 14.11.2023.

Candidate: Assist. Prof. Dr. Hristina Ilieva Dimitrova, Institute of Mineralogy and Crystallography - BAS

Member of the Scientific Jury: Prof. Dr. Mihail P. Tarassov, Institute of Mineralogy and Crystallography – BAS

Dr. Hristina Ilieva Dimitrova, Assistant Professor in the same institute, is the only candidate in the competition. The documents presented by the candidate for participation in the competition meet the regulatory requirements of the "Law on the Development of Academic Staff in the Republic of Bulgaria, the Implementing Regulations of the Law (IRLAS), the BAS Regulations (BRAS), and the Regulations for the conditions and order for acquiring scientific degrees and for taking up academic positions at IMC-BAS. Hristina Dimitrova completed her higher education in 2005 at Sofia University "St. Kliment Ohridski" with a Master's degree in "Ecology and Environmental Conservation". Her active research development started in 2012, resulting in her obtaining a PhD degree in 2018. She has worked as an assistant and since 2019 to the present as a Senior Assistant at IMC-BAS.

Dr. Hristina Dimitrova participates in the competition with 23 publications, of which 20 are in refereed international journals with impact factor or having SJR. The publications are divided to cover the indicators related to the minimum national requirements specified in the IRLAS and BRAS. For covering indicators from Group B, five publications are allocated, one in Q1 (journal Chemo-Biological Interactions) and four in Q2 (journal Crystals), with a total of 105 points, with the minimum requirement being 100 points. The remaining publications cover the indicator for Group Г (268 points with a minimum requirement of 220 points), six in Q1, one in Q2, two in Q3, four in Q4, and two with SJR without IF (8, 9). Publications 8 and 9 are counted as 10 points, and publications 5, 7, and 14 are not scored for the Professional field 4.3. Biological Sciences. For compliance with Group D indicator (Citations in scientific publications...), Dr. Hristina Dimitrova has presented 83 citations (170 points) for 14 publications, exceeding the minimum requirements of 50 points. According to Scopus (authorId=56115110900), her Hirsch index (h) is 5 (excluding self-citations, etc.). The most cited publication is the one with a developed preparative protocol for the preparation of bacteria for observation with scanning electron microscopy. Thus, according to the texts of the above-mentioned regulatory documents (law and regulations), the candidate Dr. Hristina Dimitrova meets the minimum requirements for the academic position of "Associate Professor".

In addition to the minimum national requirements required by Article 2 of the IRLAS for candidates for the academic position of "Associate Professor", Dr. Hr. Dimitrova has participated in 15 national and international scientific events, congresses, conferences, schools, etc., including 14 poster presentations in co-authorship and one report. She has actively participated in several national and international projects covering topics such as crystal growth of DNA, the structure of DNA and proteins, studies of newly synthesized derivatives of memantine with potential for Alzheimer's disease prevention, co-crystallization of promoter sequences of the amyloid precursor protein (APP) gene in Alzheimer's disease with Thioflavin T and other fluorescent markers. She is the leader of one project

funded by the National Science Fund and a participant in three more. These activities highlight her skills in organizational and scientific planning, revealing her active role in research activities.

The scientific activity of the candidate can be classified into two main directions: research related to the crystallization of nucleic acids and proteins with a view to clarifying their interactions with ligands and fluorescent markers, and applied-oriented activity:

- Dr. Dimitrova has crystallized and solved (with diffraction techniques) the structure of the DNA sequence 5'-GCCACACGGC-3' registered for the first time in PDB under number 8ASK with a resolution of 296 Å, characterized by a B-DNA conformation. In the Protein Data Bank (PDB), the structures 5JU4, 5NT5, 5T4W, 8ASH, and 6G5C are also deposited.
- She has successfully optimized the crystallization of DNA sequences from the promoter region of the APP gene, including their co-crystallization with Thioflavin T and other fluorescent markers.
- She has studied the interaction of oligonucleotide sequences with fluorescent markers such as DAPI, Berenil, and other ligands, having co-crystallized the DNA sequences with the markers, and in some cases reaching crystals diffracting to a resolution of 1.84 Å. The structural analysis reveals interactions and variations in DNA, for example, with an A-DNA form.
- She obtained a DNA structure with a new homolog of Thioflavin, 2-((4-(dimethylamino)benzylidene)amino)-3,6-dimethylbenzo[d]-thiazol-3-ium iodide, where the interaction documented through FID was confirmed with X-ray structural analysis.

A major, possibly applied, contribution is the work related to the development of a "Simple and Fast Methodology for the Preparation of Biological Samples: Application on Bacteria and DNA Samples for Observation with Scanning Electron Microscopy". In summary, the development includes a rapid preparation procedure that allows the visualization of biological samples such as DNA and bacteria through scanning electron microscopy (SEM). The procedure involves fixing the samples followed by sequential dehydration and processing for electron microscope observation. The fixation step is performed by allowing the samples to embed in an agarose matrix. Dehydrating the samples ensures they do not degrade during SEM processing or in the SEM vacuum chamber. The entire process can be completed within 6–24 hours and is optimized for visualizing bacteria and DNA. Once processed for SEM, samples can be stored under mild vacuum for weeks, allowing ample time for image acquisition. Additionally, the methodology offers an alternative to traditional, longer procedures that use harmful chemicals (osmium, glutaraldehyde) for preparing biological samples for SEM.

I have no critical remarks or questions regarding the materials presented for the competition.

The brief analysis of the works with which Senior Assist. Dr. Hristina Dimitrova presents herself convincingly demonstrates the high scientific value of her results. Based on the presented documents, it can be concluded that Dr. Hristina Dimitrova is an established independent researcher with clearly defined scientific themes that she develops in-depth. I support her candidacy and recommend to the members of the Scientific Jury to propose to the Scientific Council of IMC-BAS to elect Dr. Hristina Dimitrova to the academic position of "Associate Professor" in the professional field 4.3. Biological Sciences (Crystallization and Structural Analysis of DNA and Proteins).

16.03.2024

Sofia

/ Prof. Dr. Mihail Tarassov /